

# Sensitivity of *Neisseria gonorrhoeae* to spectinomycin and thiamphenicol

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**SUMMARY** Between 1966 and 1978 the sensitivities of strains of *Neisseria gonorrhoeae* (70-80 strains in each year) to penicillin, thiamphenicol, and spectinomycin were tested. For penicillin the proportion of less sensitive strains increased from 21% in 1976 to 41% in 1978 and for thiamphenicol from 10% to 18% over the same period. All the strains proved to be sensitive to spectinomycin. A significant correlation in the degree of sensitivity was observed between penicillin and thiamphenicol but not between penicillin and spectinomycin.

## Introduction

All over the world strains of *Neisseria gonorrhoeae* have shown a steady reduction in sensitivity to penicillin. This situation demands the continued development of suitable alternatives for the treatment of gonorrhoea.

In 1976 in Lübeck the situation was relatively favourable with only 21% less sensitive strains ( $IC_{50}$  0.063 IU/ml) (fig 1).<sup>1</sup> In 1977 this proportion increased to 31% and in 1978 to 41%; the graph shows the higher peaks moving to the right (fig 1). The increase in mean 50% concentration ( $IC_{50}$ ) from 0.08 IU/ml to 0.19 IU/ml is significant ( $t=3.4732$ ;  $P<0.001$ ). Consequently, conditions here are now similar to those observed in other regions some years ago.<sup>2,3</sup>

Although the so-called less sensitive strains can still be treated with larger doses of penicillin, the limit of effectiveness of penicillin will be reached in a few years' time if this trend persists. In addition, there have been reports from a number of countries in the last three years of  $\beta$ -lactamase-producing strains with an absolute resistance to penicillin.<sup>4-15</sup>

For these reasons we have tested the sensitivity of strains isolated in the Lübeck area (preserved since 1976 in liquid nitrogen) to spectinomycin and thiamphenicol and compared the results with their sensitivity to penicillin.

## Materials and methods

The sensitivity of strains to spectinomycin and thiamphenicol was determined by the plate dilution

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Received for publication 24 September 1979

method according to the directions of the WHO International Reference Centre for Gonococci in Copenhagen.<sup>16</sup> The evaluation was performed by the Kärber method and a mean  $IC_{50}$  was calculated.<sup>16</sup>

## STATISTICAL ANALYSIS

Student's  $t$  test was used to compare differences of antibiotic sensitivity in the different years. Where correlations between two antibiotics were obvious we used the non-parametric graphical medial test, as described by Quenouille;<sup>17</sup> where correlations were doubtful a rank correlation method with ties (Spearman) was performed.<sup>18</sup>

## Results

The sensitivity of the strains to spectinomycin and thiamphenicol over the three-year period is shown in fig 2. Between 1976 and 1978 the mean  $IC_{50}$  of spectinomycin increased slightly but significantly from 7  $\mu$ g/ml to 8.5  $\mu$ g/ml ( $t=3.6608$ ;  $P<0.001$ ). Although the peak remained at 10  $\mu$ g/ml the percentage of strains sensitive to 10  $\mu$ g/ml increased. None of the strains, including a  $\beta$ -lactamase-producing strain imported from Manila and examined in our laboratory, exceeded the limit of 10  $\mu$ g/ml. Therefore all the strains must be regarded as highly sensitive. The asymmetrical distribution with the maximum peaks at the right side corresponds with the results of other studies.<sup>19-23</sup>

The mean  $IC_{50}$  of thiamphenicol increased significantly from 0.21  $\mu$ g/ml to 0.34  $\mu$ g/ml ( $t=4.4188$ ;  $P<0.001$ ); the peak shifted to the right approximately according to the penicillin distribution. The proportion of less sensitive strains increased from 10% in 1976 to 18% in 1978. In 1978, two strains had an  $IC_{50}$  of 1.41  $\mu$ g/ml and must be

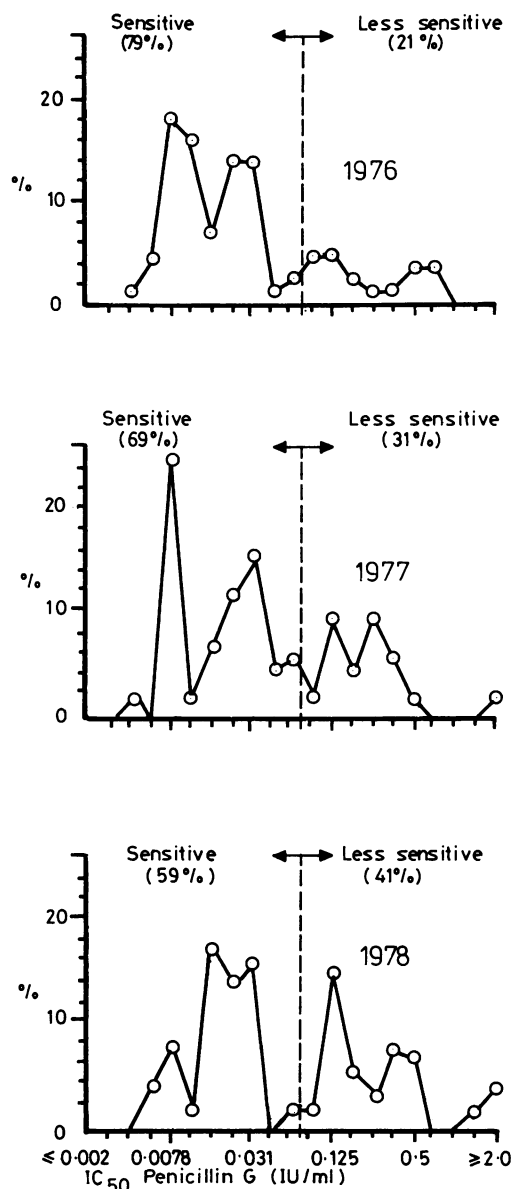


FIG 1 Sensitivity of strains of *N. gonorrhoeae* to penicillin in the Lübeck area in 1976, 1977, and 1978.

regarded as resistant (one of them was the  $\beta$ -lactamase-producing strain mentioned above).

The correlation of spectinomycin and thiamphenicol sensitivities with those of penicillin for all strains isolated in the three years with 228 pairs of observations are shown in fig 3. The correlation with penicillin was not significant for spectinomycin but was significant for thiamphenicol, as also reported by other authors.<sup>20</sup> Although the regression line on

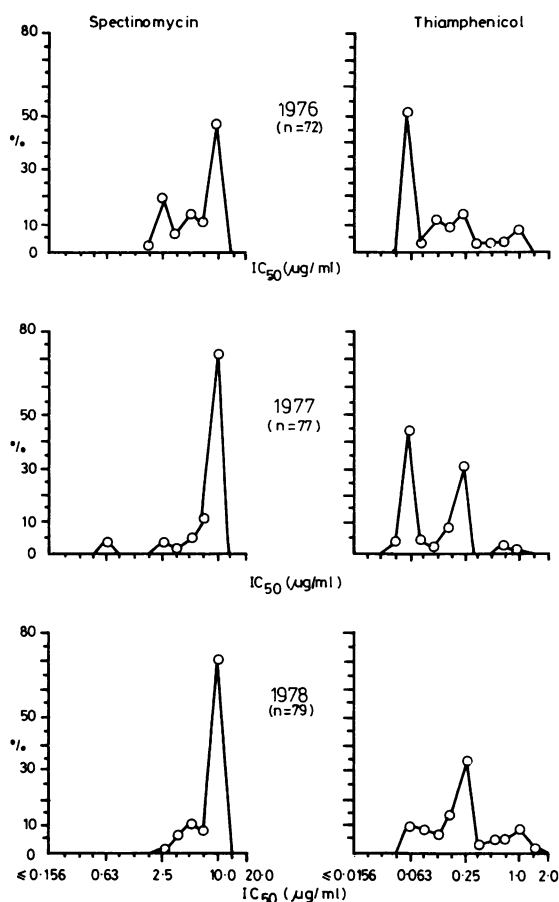


FIG 2 Sensitivity of strains of *N. gonorrhoeae* to spectinomycin and thiamphenicol in the Lübeck area in 1976, 1977, and 1978.

the graph has visual impact, it is not quite correct since the values are not normally distributed. In the statistical evaluation of the correlation between penicillin and thiamphenicol we therefore used the non-parametric graphical medial test and found the correlation was significant at the 1% level.

The correlation between penicillin and spectinomycin proved not to be significant by Spearman's rank correlation with ties ( $r_s^* = 0.024$ ;  $2\alpha > 0.1$ ).

## Discussion

Our investigation of the sensitivities of strains of *N. gonorrhoeae* to two alternative antibiotics showed that both were suitable in cases where penicillin treatment was unsuccessful or, for other reasons, impossible.

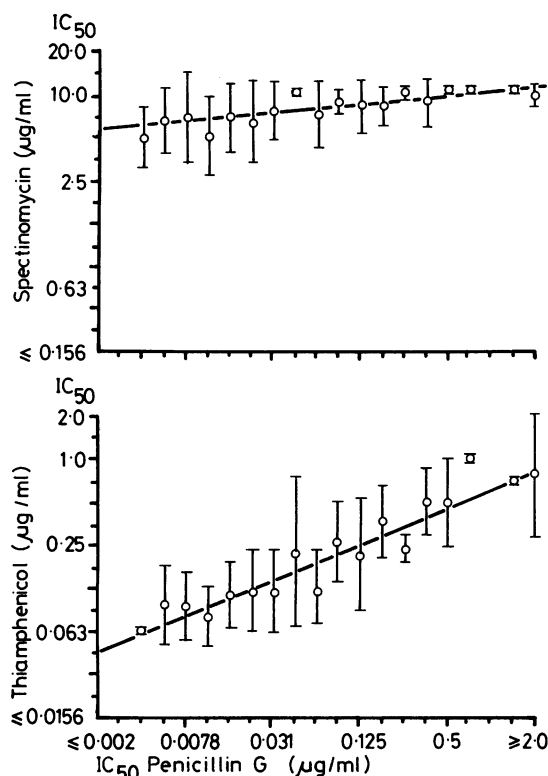


FIG 3 Correlation of sensitivities to spectinomycin and thiamphenicol with those to penicillin showing mean values with their standard deviation.

Sensitivity to thiamphenicol was significantly correlated with that to penicillin, but the proportion of less sensitive strains was significantly smaller—8% for thiamphenicol compared with 41% for penicillin in 1978.

In an appraisal of spectinomycin the following points should be considered:

- (1) An increase of mean  $IC_{50}$  occurred during the three-year period, but it was insignificant.
- (2) The proportion of less sensitive strains did not increase.
- (3) The margin of therapeutic action is still considerable, assuming that the breakpoint for sensitive bacteria is  $30 \mu\text{g/ml}$ .
- (4) Because the correlation with penicillin sensitivity was insignificant a marked change in the present favourable situation should not be expected in the near future.

Periodic investigation of sensitivity to spectinomycin is indicated, particularly to recognise an increasing resistance of the "one-step" type.

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